REMARKS

Applicants request entry of this Amendment and reconsideration of the rejection of the claims.

With entry of this Amendment and Response, claim 11 and 98 are canceled. Applicants reserve the right to pursue the subject matter of these claim in one or more continuation applications.

Claims 9, 15, 96, 99, 102, 103 and 106 are amended. It is our understanding that the Examiner was unable to locate the support for claim amendment language in the specification. Applicants will identify the locations for support in the published patent application 2002/0156252. The amendments are supported throughout the specification, including at paragraphs 0031, p 4-5; 0113, p 13; 0114, p 13; 0115, p 13; 0096, p 11; and 0131, p15 of the published application 2002/0156252.

Applicants have added new claims 107-112. Applicants submit the claims are supported throughout the specification, including at paragraph 0087, p 9.

Priority

Applicants' claim for domestic priority under 35 U.S.C. § 119(e) to U.S. Serial No. 60/228,914, filed August 29, 2000, U.S. Serial No. 60/197,089, filed April 14, 2000 is acknowledged by the Office. Applicants request acknowledgement of the claim for domestic priority to U.S. Serial No. 60/175,849 filed, January 13, 2000. As stated in the previous Response, Applicants teach the specific nucleotide of SEQ ID NO:1 and amino acid sequence of SEQ ID NO:2 at, *inter alia*, page 14, lines 17-24; and Figures 1 and 2, respectively, of U.S. Serial No. 60/175,849.

IDS Submissions

The Supplemental IDS statements on Sept. 12, 2001 and March 31, 2005 have been acknowledged by the Office. Applicants have not received an acknowledged copy of the IDS submitted on October 20, 2004. A courtesy copy of the IDS submitted on October 20, 2004 is attached. Applicants request consideration of all of the references and return of the initialed 1449 form.

35 U.S.C. § 112, First Paragraph, Written Description

Claims 96, 99, and 100-106 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. We understand the Examiner to have several bases for the rejection including:

1) The Examiner alleges there is insufficient description to support claims drawn to polynucleotides having 99% identity with a DNA encoding a polypeptide comprising an amino acid sequence of amino acids 1 to 667 of Figure 2 and having nine potential transmembrane domains, or polynucleotides comprising DNA having at least 99% sequence identity with nucleotide positions 49-2049 of SEQ ID NO:1. (See the Office Action at page 2, Section 3A)

2) The Examiner also contends that there is no written description of epitopes recognizable by an antibody raised against a protein comprising an amino acid sequence of SEQ ID NO:2 and thus no description of the genus of polypeptides that would bind the antibody. (See the Office Action at page 4, Section 3B)

3) The Examiner also contends that, with respect to claim 96, that the specification does not describe a genus of nucleic acids with 99% identity to a DNA encoding a polypeptide of SEQ ID NO:2 and which encodes the identified domains. The Examiner also contends that there is no basis in the specification for one of the domains (amino acids 512-531). (See the Office Action at page 5, Section 4)

4) The Examiner contends the specification does not teach an antibody raised against a PRO10282 polypeptide comprising an amino acid sequence of 532 to 667 of SEQ ID NO:2 and does not teach an isolated nucleic acid which encodes a polypeptide which binds to the antibody. (See the Office Action at page 6, Section 5)

Applicants respectfully traverse.

The written description requirement requires that Applicants' specification must convey with reasonable clarity to those skilled in the art that, as of the filing sought, he or she was in possession of the invention. Vas-Cath, Inc. v. Mahurkar, 19 USPQ2d 1111,

1116 (Fed. Cir. 1991). Moreover, as noted in the Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, ¶ 1, "Written Description" requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed. Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90, 97 (CCPA 1976). The guidelines further state that "[(The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize an applicant's disclosure of a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398. 1405 (Fed. Cir. 1997). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. *Id.* at 1406 Applicants can also satisfy the written description by providing partial structure, physical and chemical properties, functional characteristics, known or disclosed correlation between structure and function, methods of making and combinations thereof. (See the Guidelines for Written Description at page 8.)

The Examiner contends that the specification lacks written description for claims directed to an isolated nucleic acid molecule comprising DNA having 99% sequence identity to a DNA molecule encoding a polypeptide comprising the amino acid sequence of amino acids 1 to 667 of Figure 2, wherein the nucleic acid encodes a polypeptide that has amino acid sequence of certain domains, or a DNA molecule having at least 99% sequence identity with nucleotide positions 49 to 2049 of SEQ ID NO:1. Applicants respectfully traverse.

Claim 96 is directed to polynucleotides having 99% sequence identity with a DNA encoding a Stra6 polypeptide, wherein the isolated nucleic acid encodes a polypeptide having amino acids corresponding to defined regions of SEQ ID NO:2, and a

complement thereof. Claim 99 is directed to a nucleic acid having 99% sequence identity with the cDNA deposited as PTA-1181, wherein the nucleic acid encodes a polypeptide having amino acids of regions of a polypeptide comprising SEQ ID NO:2. Claims 100 and 101 depend from claims 96 and 99, and are directed to vectors and host cells. Claim 102 is directed to a nucleic acid having at least 99% sequence identity with a DNA encoding a polypeptide comprising an amino acid sequence of amino acids 1 to 667 of SEQ ID NO:2, wherein the isolated nucleic acid encodes a polypeptide that binds an antibody against a Stra6 polypeptide comprising the sequence of amino acid residues 532 to 667 of SEQ ID NO:2 and which is expressed on the cell surface. Claim 103 parallels claim 102 for polynucleotides having 99% sequence identity with the human cDNA deposited as PTA-1181. Claim 106 is directed to a polynucleotide having 99% sequence identity with a polynucleotide corresponding to nucleotides 49 to 2049 of SEQ ID NO:1, and which encodes an active Stra6 polypeptide, or the complement thereof.

Applicants submit the specification as filed provides adequate written description for the rejected claims. As an initial matter, the examiner has acknowledged that the specification provides written description and enablement for a polynucleotide comprising a sequence of SEQ ID NO:1 .

Further, Applicants have provided the structure of polynucleotides comprising SEQ ID NO:1, and SEQ ID NO:4 (see Figures 1 and 6) and the structure of polypeptides comprising an amino acid sequence of SEQ ID NO:2 and SEQ ID NO:5 (see Figures 2 and 3). One of the polypeptides is a variant of the other and has at least 99% sequence identity to the other polypeptide. Applicants have provided further characterization of each of the polypeptide sequences by identifying transmembrane domains, N-glycosylation sites and N-myristoylation sites (see paragraph 0028 (p.4), Figures 2 and 7). Applicants have shown that a human Stra6 polypeptide is on the cell surface of human colorectal cancer cells as determined by antibody staining. (See the specification at paragraph 0497 of publication US 2002/156252 A1, p 53).

Moreover, the alignment between the amino acid sequence (SEQ ID NO:2), the amino acid sequence of the variant (SEQ ID NO:4), and the murine stra6 sequence

further identifies conserved regions of the molecules. (See Figure 8 and description at paragraphs 0168 and 0383 in corresponding US Application Publication 2002/156252 A1.) Given the structural characterization, as well as the physical chemical properties, in particular, the identification of Stra6 as a cell surface protein, one of skill in the art would understand that Applicants have described the genus of nucleic acids that have 99% sequence identity to a DNA molecule encoding a polypeptide comprising the amino acid sequence of amino acids residues 1 to 667 of Figure 2 and wherein the nucleic acid encodes an active Stra6 polypeptide, an active Stra6 polypeptide that binds an antibody specific for amino acids 537-667 of polypeptide of SEQ ID NO:2, or an active Stra6 polypeptide that comprises an amino acid sequence of certain defined regions. The alignment between the two human proteins and the mouse protein provided by the specification would readily allow one of skill in the art to identify other changes can be made to the molecule.

In addition, at paragraph 0096, p 11 in the published application, the specification states "PRO10282(Stra6) variant nucleic acid sequence" means a nucleic acid which encodes an active PRO10282 polypeptide as defined below and which has at least about 80% nucleic acid sequence identity with either (a) a nucleic acid molecule which encodes residues 1 to 667 of the PRO10282 polypeptide shown in Figure 2 (SEQ ID NO:2).....(emphasis added) An active PRO10282 (Stra6) polypeptide is described in the specification at paragraph 0131 (p 15) as forms of PRO10282 (Stra6) which retain a biological or immunological activity of native or naturally occurring PRO10282 (Stra6).

Applicants submit that they have described methods of making an antibody and an antibody that binds to a native PRO10282 (Stra6) polypeptide expressed on the cell surface at paragraphs 0323-0353 (p 35-39) and 0429 (p 46) in the published application. Applicants have further described the production of monoclonal antibodies that bind to a native PRO10282 (Stra6) polypeptide and were raised by immunizing with a polypeptide of amino acids 532 to 667. See specification at paragraph 0429 (p 46). Applicants have demonstrated that antibodies raised against Stra6 polypeptide detect a Stra6 polypeptide expressed on the cell surface of colorectal cancer cells. (See paragraph 0497, p 53.)

Applicants submit one of skill in the art reading the specification would understand that Applicants have described the genus of isolated nucleic acids comprising a DNA that has 99% sequence identity to a DNA molecule encoding an amino acid sequence of 1 to 667 of Figure 2 (SEQ ID NO:2) and that encodes an active PRO10282 (Stra6) polypeptide.

With respect to a nucleic acid that encodes a polypeptide that has the amino acid sequence of specified domains, Applicants submit that the variant nucleic acid can encode an active PRO10282 (Stra6) polypeptide. An active PRO10282 (Stra6) retains a biological activity of native or naturally occurring PRO10282. Applicants submit that they have described the domain structure of human Stra6, that human Stra6 is present on the cell surface of colorectal cancer cells and that cell surface expression increases upon treatment of the cells with a retinoid. (See the specification at 0497, p 53) Thus, Applicants submit one of skill in the art reading Applicants' specification would understand the specification to include variant nucleic acids encoding an active PRO10282 (Stra6) polypeptide comprising the amino acid sequence of the domains of the polypeptide comprising SEQ ID NO:2.

Applicants request withdrawal of the §112, first paragraph rejection of claims 96, 99 and 100-106 on this basis.

2) The Examiner also contends that there is no written description of epitopes recognizable by an antibody raised against a protein comprising an amino acid sequence of SEQ ID NO:2 and no description of the genus of polypeptides that would bind the antibody. Applicants traverse.

As an initial matter, Applicants submit that in order to satisfy written description of an antibody that would bind to a polypeptide comprising an amino acid sequence of SEQ ID NO:2, it is not necessary to identify the epitopes that the antibody binds to. Applicants submit that the written description guidelines provide that a well characterized antigen provides adequate written description. (See written description guidelines at pages 59-60;Example 16) Applicants have provided the sequence of Stra6 polypeptide comprising SEQ ID NO:2 and have demonstrated that a polypeptide comprising amino

acids 537 to 667 can be used to prepare monoclonal antibodies. In addition, monoclonal antibodies that are specific for human Stra6 can detect the expression of the protein on the cell surface. (See the specification at 0497, p 53.) Applicants submit the characterization of the antigen and description of antibodies that can bind to Stra6 is sufficient written description to support at least claims 102-103.

Applicants respectfully request withdrawal of the rejection on this basis.

3) The Examiner also contends that, with respect to claim 96, that the specification does not describe a genus of nucleic acids with 99% identity to a DNA encoding a polypeptide of SEQ ID NO:2 and which encodes the domains and that there is no basis in the specification for one of the domains (amino acids 512-531). Applicants respectfully traverse.

As discussed previously, the specification does describe variants of a nucleic acid that encode a polypeptide comprising an amino acid sequence of SEQ ID NO:2 and that encode an active Stra6 polypeptide. (para 0096, p 11.) The specification also provides that an active Stra6 polypeptide retains a biological or immunological activity of native or naturally occurring polypeptide. Applicants submit that they have also described the location of the transmembrane domains in human Stra6, that it is expressed on the cell surface, and is upregulated in response to retinoic acid. Moreover, Applicants have isolated a polypeptide encoding a Stra6 polypeptide that is encoded by a polynucleotide that has at least 99% identity to a DNA molecule encoding a polypeptide comprising an amino acid sequence of SEQ ID NO:2. Applicants submit one of skill in the art reading the specification would understand that Applicants have possession of the claimed invention. Applicants respectfully request withdrawal of the rejection on this basis.

Moreover, the Examiner contends that the identification of the amino acid sequence of 512 to 531 is new matter. Applicants direct the Examiner's attention to the specification at para 0028 (p 4) where the transmembrane domains are described. Applicants respectfully submit Applicants have described transmembrane domains and that this is not new matter. Applicants request withdrawal of the rejection.

4) The Examiner rejected claims 102 and 103 as including new matter. Applicants respectfully traverse.

As discussed previously, Applicants have described a variant nucleic acid that has 99% sequence identity to a DNA molecule encoding a polypeptide comprising an amino acid sequence of SEQ ID NO:2 and that encodes an active Stra6 polypeptide. (para 0096, p 11) An active Stra6 polypeptide retains at least one biological or immunological function of a native or naturally occurring Stra6 polypeptide. (para 0131-0132, p 15) Applicants have described raising monoclonal antibodies to an amino acid sequence of 532 to 667 of SEQ ID NO:2. (See the specification at para 0429, p 46.) Applicants have further described that monoclonal antibodies to a human Stra6 protein detect expression of Stra6 on the cell surface of a colorectal cancer cell and that such expression is enhanced in response to retinoic acid. (para 0497, p 53)

Applicants submit that contrary to the Examiner's position, they have described and supported the subject matter of claims 102 and 103 and have not introduced new matter.

Applicants respectfully request withdrawal of the rejection on this basis.

Applicants submit the specification provides sufficient written description to show possession of the claimed invention, and respectfully request withdrawal of the 35 U.S.C. § 112 first paragraph rejection.